



PATENT

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Dated: June 10, 2008

BY:


Rodney D. DeKruif

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Emrick et al.

Serial No: 10/643,015

Filed: August 18, 2003

For: PYRIDINE AND
RELATED LIGAND
COMPOUNDS,
FUNCTIONALIZED
NANOPARTICULATE
COMPOSITES AND
METHODS OF
PREPARATION

Attorney Docket No. 7163

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RULE 131 DECLARATION OF HABIB SKAFF

1. I, Habib Skaff, am a co-inventor with regard to the invention (the "Invention") disclosed and claimed in the above-entitled application (the "Application"). I make this declaration in support of the Application and, in particular, to antedate a reference cited against the Application.

2. The Invention claimed in the Application was completed before the effective date of application serial number 10/219,440 (*i.e.*, the Dubertret

reference). More specifically, the Invention was conceived and with due diligence reduced to practice, in this country--the United States of America, prior to the effective date of the Dubertret reference.

3. This Declaration, and prior invention, is supported by copies of pertinent pages from my laboratory research notebook, entries to which I contemporaneously signed and dated and were witnessed by co-inventor, Todd S. Emrick. Date redacted copies of the aforementioned notebook pages are provided collectively as Exhibit A and incorporated herein by reference. These documents establish that the Invention was made at least as early as June 1, 2002, which is a date earlier than the effective date of the Dubertret reference.

4. More specifically, as part of my graduate research work with co-inventor Emrick, I prepared composites of a metallic nanoparticulate component coupled to a polymeric ligand component. For purposes relating to our research, we referred to such a nanoparticulate as a nanocrystal, abbreviated "Nc". Preparation of such a nanoparticulate, Nc, composite is evidenced on page 37 of Exhibit A, and the composite recorded therein was prepared at least as early as June 1, 2002.

(a) Representing a range of available nitrogen-containing moieties, I used a pyridinyl group to couple the ligand and nanoparticulate components. Coupling of such ligand and nanoparticulate components is evidenced on page 37 of Exhibit A, and the coupling recorded therein was achieved at least as early as June 1, 2002.

(b) Representing a range of available nanoparticulate components, I used CdSe. Use of such a nanoparticulate is evidenced on pages 37-38 of Exhibit A, and the nanoparticulate recorded therein was used at least as early as June 1, 2002.

(c) Representing a range of available polymers, I used poly(ethylene glycol) to prepare such a polymeric ligand component. Preparation of such a ligand component, including coupling to a pyridinyl moiety, is evidenced on pages 14-15, 23, 25 and 37 of Exhibit A, and the ligand recorded therein was prepared at least as early as June 1, 2002.

(d) Representing a range of available terminal functional groups, I chose a hydroxy group to terminate poly(ethylene glycol). Preparation of such a hydroxy-terminated polymeric ligand component, and subsequent coupling with a nanoparticulate, is evidenced on pages 15 and 37 of Exhibit A, and the ligand recorded therein was prepared and used at least as early as June 1, 2002.

5. As a related part of my graduate research with co-inventor Emrick, I also prepared systems for nanoparticulate dispersion. As part of such a system, I prepared a composite of a metallic nanoparticulate component (Nc) and a ligand component in a liquid medium: a representative nanoparticulate component, CdSe, was coupled to a tri-n-octyl phosphine oxide (TOPO) ligand component, then dissolved in tetrahydrofuran (THF). Preparation of such a composite of a ligand component in a liquid medium is evidenced on page 38 of Exhibit A, and

the composite in liquid medium recorded therein was prepared at least as early as June 1, 2002.

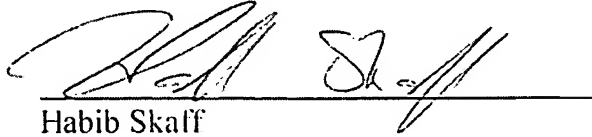
(a) The system I prepared also included another ligand component in another liquid medium. Representative of many available ligands and as described above, I used a ligand of poly(ethylene glycol) with a pyridinyl coupling moiety, and I showed this ligand to be soluble in water. Ligand preparation and water solubility is evidenced on page 15 of Exhibit A, and the ligand recorded therein was prepared and dissolved at least as early as June 1, 2002.

(b) To demonstrate this dispersion system, I precipitated the CdSe-TOPO composites out of THF solution. To demonstrate greater nanoparticulate affinity for another ligand component, the CdSe-TOPO composites were redissolved in a water medium containing pyridinyl/poly(ethylene glycol) ligand components. With dissolution of the nanoparticulates in water, I showed that the pyridinyl/poly(ethylene glycol) ligand components have greater affinity for the CdSe nanoparticulates than the TOPO ligand components. This dispersion system, showing greater nanoparticulate affinity of one ligand component over another, is evidenced on page 38 of Exhibit A, and the system for nanoparticulate dispersion recorded therein was demonstrated at least as early as June 1, 2002.

I hereby declare that: All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be

true; that those statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code; and that willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

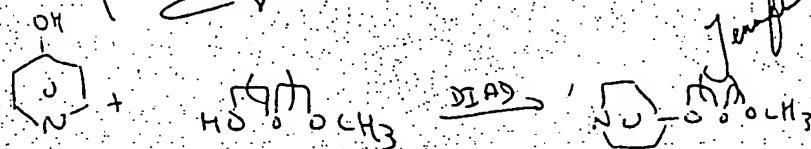
Date 6/5/08


Habib Skaff

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Jeffrey M. Jacobs 3

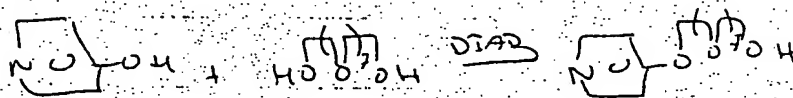


Reagents

- | | | | |
|-----|---|------------------------|----------------------------|
| 95 | ① | <chem>Oc1ccncc1</chem> | 2g, 0.022 mol |
| | ② | | |
| 75 | ② | m-Py H ₂ O | 14.25g, 0.019 mol |
| 262 | ③ | Ph ₃ P | 6.28g, 0.024 mol |
| 222 | ④ | DIAD | 4.84g, 0.024 mol (4.72 mL) |
| | ⑤ | THF (dry) | 300 mL 250 mL |

Procedure

- ① Ph₃P + THF loaded into 2-neck flask & stirred under N₂ @ r.t.
- ② DIAD added via syringe & stirred for 1/2 hr.
- ③ phenol & alcohol added & stirred
- ④ reacted overnight
- ⑤ extracted off THF
- ⑥ added 4 DIAD & ether → washed w/ ether
- ⑦ extracted product out w/ CH₂Cl₂ out of AA phase → MgSO₄, Rotavap
- sample show some Oc1ccncc1 → try redissolving in d. didn't work
- basic solution & precipitate into CH₂Cl₂ (cold)
- can column elute w/ CH₂Cl₂: di. ether (7:3:0), (7:2:1)



Reagents

450 ① $\text{N} \begin{array}{c} \diagup \diagdown \\ \text{C} \text{---} \text{O} \text{H} \end{array}$ & 2g, 0.011 mol

400 ② $\text{HO} \begin{array}{c} \diagup \diagdown \\ \text{C} \text{---} \text{O} \text{H} \end{array}$ 22g, 0.055 mol
p=1.03

202 ③ DIAO 2.63g, 2.55 mL 0.013 mol

262 ④ Ph_3P 3.41g, 0.03

⑤ THF (an) 300 mL

Procedure

① Ph_3P + THF loaded into 3-neck 500 mL round bottom
stirred @ rt under N_2

② DIAO added via syringe & stirred for 1 hr

③ phenol & ~~THF~~ added & stirred

→ reacted over night

- & evaporated off all THF → note

- extracted w/ H_2O → then aqueous wash

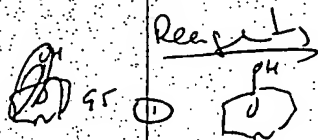
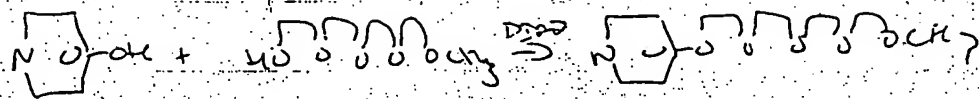
- w/ CH_2Cl_2 → too difficult to purify by column

→ & evaporated off CH_2Cl_2 → dissolved in H_2O ,

washed w/ ether, then Toluene → doesn't work well if

→ try acidifying aqueous to make pyridine salt

which will not be soluble in



5g, 0.055 g/mol

128 ① m-Tf

5.632g, 0.044 mol

1.02526 ② Ph₃P

13.1g, 0.05 mol

202 ③ DDA

10.1g, 0.05 mol, 9.85 mL

④ THF (dry)

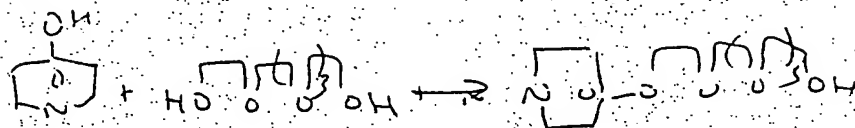
~~25 mL~~ 400 mL

Procedure

① ~~5.632g~~ Ph₃P & THF loaded into 2-neck flask & stirred under N₂ @ r.t.

② DDA added via syringe & stirred for 1/2 hr.

③ phenol & alcohol added & stirred overnight



Reagents

95	<chem>Oc1ccccc1</chem>	4g	0.042 mol
300	Heg	31.58g	0.105 mol
262	<chem>Ph3P</chem>	131g	0.05 mol
202	D5AD	10.1g	0.05 mol
	THF	500 mL	

Procedure

① phenol, Ph3P, D5AD, THF loaded in 2-neck & stirred @ r.t. under N_2 for 1/2 hr.

② diol added → stirred overnight

rotavap at THF
 → 1st column eluting w/ ① CHCl3: H_2O (20:1) ③ CHCl3: H_2O (75:20:5)
 → 2nd column eluting w/ ① CHCl3: H_2O (7:2:1)

stirred distilling off unreacted diol @ 224 °C @ 600 mtorr → didn't work well

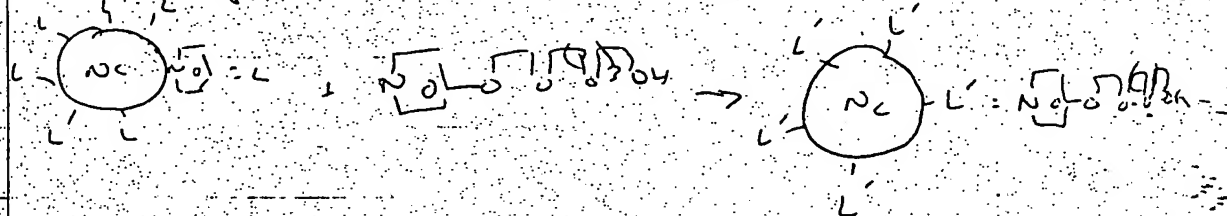
→ 3rd column in CHCl3: H_2O (75:20:5), (75:20:5), (80:20:10)

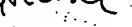
Paul R. M.

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Exchange to hex-methoxydimethyl ether

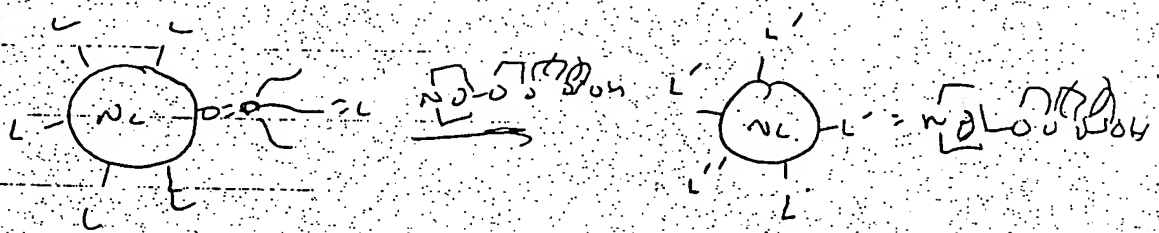
Page 1

- ① ZINCALONE NC ~ 40mg
②  600mg
③ THC (dry) 3mL
④ DIW 6mL

Procedure

- 1) 20 mg NC dispersed in solution of 300 mg
 new ligand in THF \rightarrow immediately went
 into solution
 2) dried under N_2 flow and added 3 mL
 DIW \rightarrow ^{most} ~~some~~ went into solution \rightarrow centrifuged
 3) 20 mg NC dispersed in solution of 300 mg
 new ligand in 3 mL DIW \rightarrow NC went into
 solution \rightarrow centrifuged *transfer & remove*

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Reagents

- ① TOPD (covered Ni) ~ 15mg
- ② $\text{Ni}(\text{acac})_2 \cdot 2\text{H}_2\text{O}$ 320 mg
- ③ THF (dry) 3 mL

Procedure

- ① Ni made as usual & washed w/ MeOH 3 times
- ② dried over N_2 flow
- ③ redissolved in new ligand in THF and allowed to stand over head of N_2 overnight
- ④ distilled at $1/2$ THF \rightarrow precipitated w/ hexane \rightarrow all Ni precipitated
- ⑤ washed w/ hexanes \rightarrow centrifuged \rightarrow redissolved in H_2O

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